```
=> file hca;d que l9
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FILE COVERS 1967 - 26 Aug 1995 (950826/ED)  VOL 123 ISS 9

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 for details.


L1          2639 SEA FILE=HCA (ALPHA(1A)INTERFERON)/IT
L2            29 SEA FILE=HCA HAUPTMANN RUDOLF/AU
L3             6 SEA FILE=HCA L1 AND L2
L4         29763 SEA FILE=HCA INTERFERON#/IA,IT,ST
L5         33396 SEA FILE=HCA PLASMID AND EPISOME/IT
L6         61528 SEA FILE=HCA L5 OR (PLASMID# OR EPISOME#)/IA,IT,ST
L7           984 SEA FILE=HCA L4 AND L6
L8             3 SEA FILE=HCA L7 AND (142192-09-4 OR 142192-09-4D OR 14219
                 2-09-4P)
L9             2 SEA FILE=HCA L8 NOT L3

=> d bib abs hitrn 1-

L9   ANSWER 1 OF 2  HCA  COPYRIGHT 1995 ACS
AN   117:169442  HCA
TI   Manufacture of O-glycosylated human interferon .alpha.
IN   Adolf, Guenther; Himmler, Adolf; Ahorn, Horst Johann; Kalsner, Inge;
     Maurer-Fogy, Ingrid
PA   Boehringer Ingelheim International G.m.b.H., Germany
SO   PCT Int. Appl., 98 pp.
     CODEN: PIXXD2
PI   WO9201055 A1  920123
DS   W:  AU, CA, CS, FI, HU, JP, KR, NO, PL, SU, US
     RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
AI   91WO-EP01266  910706
PRAI 90DE-4021917  900710
     90DE-4035877  901112
DT   Patent
LA   German
AB   A human interferon .alpha. is manufd. in a glycosidated
     form by expression of the corresponding cDNA in animal cell culture.
     Expression vectors for animal cells using an SV40 replication
     origin, a cytomegalovirus promoter, and a dihydrofolate reductase
     minigene were prepd. and interferon .alpha.2c cDNA was
     introduced into them.  CHO cells were transformed with these
   plasmids and transformants challenged with methotrexate to
     amplify the plasmid.  Lines resistant to 5000 nM
     methotrexate yielded 190,000-960,000 interferon units/mL
     medium.  The purified protein was glycosidated and showed the
     expected N- and C-terminal peptides.  Glycosidation sites were
     identified.
IT 142192-09-4, Interferon .alpha.2 (human clone
     pAD19B-IFN protein moiety reduced)
        (amino acid sequence of, complete, and expression in CHO cells of
        cDNA for)
```

L9 ANSWER 2 OF 2 HCA COPYRIGHT 1995 ACS
AN 117:46559 HCA
TI Glycosidated **interferon** .alpha. manufacture with transgenic animal cells
IN Himmler, Adolf; Adolf, Guenther
PA Boehringer Ingelheim International G.m.b.H., Germany
SO Ger. Offen., 24 pp.
CODEN: GWXXBX
PI DE4021917 A1 920116
AI 90DE-4021917 900710
DT Patent
LA German
AB An expression vector for the manuf. of human **interferon** .alpha., specifically .alpha.2 or .alpha.2C, in animal cell culture to ensure normal glycosidation of the protein are described. The **plasmid** uses a cytomegalovirus enhancer and promoter coupled to a hybrid intron (cytomegalovirus donor region, Hb acceptor region) to drive expression of the cDNA. Construction of the expression vector by std. methods is described. General purpose expression vectors derived from this expression vector are also described.
IT **142192-09-4DP**, **Interferon** .alpha.2 (human clone pAD19B-IFN protein moiety reduced), O-glycosidated
142192-09-4P, **Interferon** .alpha.2 (human clone pAD19B-IFN protein moiety reduced)
(manuf. in animal cell culture of)

```
=> file hca;d que l20;d iall 1-
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 for details.


L1          2639 SEA FILE=HCA (ALPHA(1A)INTERFERON)/IT
L2            29 SEA FILE=HCA HAUPTMANN RUDOLF/AU
L3             6 SEA FILE=HCA L1 AND L2
L4         29763 SEA FILE=HCA INTERFERON#/IA,IT,ST
L10       131526 SEA FILE=HCA (ESCHERICHIA COLI OR E COLI)/IA,IT,ST
L11         1366 SEA FILE=HCA L4 AND L10
L12        53776 SEA FILE=HCA (TOXIN#)/IA,IT,ST
L13           87 SEA FILE=HCA L11 AND L12
L17          884 SEA FILE=HCA (HEAT(2A)STABLE(2A)TOXIN# OR STII OR ST11 OR
                  STABLE(2A)ENTEROTOXIN#)/IA,IT,ST
L18            3 SEA FILE=HCA L13 AND L17
L19            2 SEA FILE=HCA L18 NOT L3
L20            2 SOR L19 PY


L20  ANSWER 1 OF 2  HCA  COPYRIGHT 1995 ACS
ACCESSION NUMBER:         98:15278  HCA
TITLE:                    Cyclic GMP as the second messenger in helper
                          cell requirement for .gamma.-interferon
                          production
AUTHOR(S):                Johnson, Howard M.; Archer, Douglas L.; Torres,
                          Barbara A.
CORPORATE SOURCE:         Dep. Microbiol., Univ. Texas, Galveston, TX,
                          77550, USA
SOURCE:                   J. Immunol. (1982), 129(6), 2570-2
                          CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
CLASSIFICATION:           15-5 (Immunochemistry)
ABSTRACT:
Cyclic GMP and activators (acetylcholine, Escherichia
***coli***  heat-stable toxin) of
guanylate cyclase were capable of completely replacing the helper cell or
interleukin 2 requirement for .gamma.-interferon (IFN.gamma.)
prodn. by Lyt-1-, 2+ cells from C57BL/6 mouse spleen cells.  The cyclic
GMP help was independent of DNA synthesis or proliferation in the
IFN.gamma.-producing cells, because cyclic GMP reversed mitomycin C
blockage of IFN.gamma. prodn. but did not reverse the inhibition of DNA
synthesis.  Thus, the findings presented here are unrelated to the
question of the 2nd messenger role of cyclic GMP in the activation of
lymphocytes for DNA synthesis and cellular proliferation.  The cyclic GMP
help for IFN.gamma. prodn. was antagonized by cyclic AMP and inducers
(isoproterenol) of adenylate cyclase.
```

SUPPL. TERM: **interferon** cGMP messenger helper cell
INDEX TERM: Spleen, metabolism
(helper cell function of, in .gamma.-**interferon** formation, cyclic GMP and guanylate cyclase activities in relation to)
INDEX TERM: **Interferons**
(.gamma.-, formation of, cyclic GMP and guanylate cyclase replacement of helper cell function in)
INDEX TERM: 7665-99-8 9054-75-5
(.gamma.-**interferon** formation requirement for helper cell activity replacement by)

L20 ANSWER 2 OF 2 HCA COPYRIGHT 1995 ACS
ACCESSION NUMBER: 105:41056 HCA
TITLE: Tumor necrosis factor, compositions containing it, DNA encoding it and assay method using this DNA
INVENTOR(S): Aggarwal, Bharat Bhushan; Lee, Sang He; Goeddel, David Vannorman; Nedwin, Glenn Evan
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: Eur. Pat. Appl., 90 pp.
CODEN: EPXXDW

	NUMBER	DATE
PATENT INFORMATION:	EP-168214 A2	860115
DESIGNATED STATES:	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE	
APPLICATION INFORMATION:	85EP-0304758	850703
PRIORITY APPLN. INFO.:	84US-0628059	840705
	84US-0627959	840705
	84US-0628060	840705
	84US-0677454	841203
	84US-0677156	841203
	84US-0677257	841203

DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: C07K-003/18
SECONDARY: C07K-013/00; A61K-037/02; C12P-021/02; C12N-015/00; C12Q-001/68; A61K-045/02
INDEX: A61K-045/02, A61K-037/02
CLASSIFICATION: 15-1 (Immunochemistry)
Section cross-reference(s): 1, 3, 16

ABSTRACT:
A method for the isolation and purifn. of tumor necrosis factor (TNF) from recombinant and nonrecombinant cells is presented. Thus, human peripheral blood monocytes were induced with Staphylococcal interotoxin 3 and PMA (a tumor promoter) to produce TNF. The cell culture supernatant contained both TNF and lymphotoxin. To remove the lymphotoxin the TNF activity was batch-absorbed to controlled pore glass beads and eluted, after washing, with 20% ethylene glycol. This eluate was directly applied to a DEAE cellulose 53 column and eluted, after washing, with step up gradients of 75 mM, 150 mM, and 500 mM NaCl in 10 mM phosphate buffer. The eluate was monitored for absorbance at 280 nm and TNF activity as a function of elution fractions. The TNF active fraction was concd., dialyzed, and loaded onto a quaternary ammonium group-substituted

Sepharose bead column and the eluted, after washing, with a linear gradient of 40-75 nM NaCl in an appropriate buffer. The effluent was collected in 2 mL aliquots and monitored for absorbance at 280 nm, cond., and TNF activity. The TNF active fraction was then subjected to chromatofocusing using a Pharmacia Mono P column. One mL aliquots were collected and the absorbance at 280 nm and the pH of the effluent were measured. TNF had an isoelec. point of .apprx.5.3. The mol. wt. of TNF, as detd. by HPLC was .apprx.45,000 daltons. Plasmid vectors that contained TNF- and TNF mutant-coding sequences and that were capable of expressing those sequences in **Escherichia coli**, yeast, and mammalian cells were constructed and the nucleotide and amino acid sequences of the wild-type and mutant TNFs were presented. TNF can be used in the therapeutic treatment of malignant tumors, either alone or in synergistic combination with an **interferon**.

SUPPL. TERM: human tumor necrosis factor isolation purifn; cloning tumor necrosis factor mutant cDNA; neoplasm inhibitor tumor necrosis factor

INDEX TERM: **Escherichia coli**
Yeast
(cloning in, of tumor necrosis factor cDNA, of human)

INDEX TERM: Protein sequences
(of human tumor necrosis factor and mutants, of human, complete)

INDEX TERM: Molecular cloning
(of tumor necrosis factor cDNA, of human, in **Escherichia coli** and yeast and mammalian cells)

INDEX TERM: Alkenes, polymers
(polymers, in tumor necrosis factor isolation and purifn.)

INDEX TERM: Cytotoxic agents
Neoplasm inhibitors
(tumor necrosis factor and mutants as, genetically engineered)

INDEX TERM: Animal cell
(CHO, cloning in, of tumor necrosis factor cDNA, of human)

INDEX TERM: Glass, oxide
(beads, in tumor necrosis factor isolation and purifn.)

INDEX TERM: Mutation
(deletion, in tumor necrosis factor of human, construction of plasmids encoding)

INDEX TERM: **Toxins**
(entero-, **STII**, leader sequence of, of **Escherichia coli**, tumor necrosis factor fusion product with)

INDEX TERM: Mutation
(insertion, in tumor necrosis factor of human, construction of plasmids encoding)

INDEX TERM: Lymphokines and Cytokines
(lymphotoxins, tumor necrosis factor free of, prepn. of)

INDEX TERM: Gene and Genetic element, microbial
(promoter, of alc. dehydrogenase gene, tumor

necrosis factor expression in yeast under regulation of)

INDEX TERM: Mutation
(substitution, in tumor necrosis factor of human, construction of plasmids encoding)

INDEX TERM: Lymphokines and Cytokines
(tumor necrosis factor, of human, isolation and purifn. of, from recombinant and nonrecombinant sources)

INDEX TERM: Deoxyribonucleic acid sequences
(tumor necrosis factor-specifying, of human)

INDEX TERM: **Interferons**
(.gamma.-, tumor necrosis factor administration with, as neoplasm inhibitor)

INDEX TERM: 94948-61-5 103107-16-0 103107-17-1 103107-18-2
103107-19-3 103107-20-6 103107-21-7 103107-22-8
103107-23-9 103107-24-0 103107-25-1 103107-26-2
103107-27-3 103107-28-4 103107-29-5 103107-30-8
103107-31-9 103107-32-0 103107-33-1 103107-34-2
103107-35-3 103107-36-4 103107-37-5 103107-38-6
103107-39-7 103107-40-0 103107-41-1 103107-42-2
103107-43-3 103107-44-4 103107-45-5 103107-46-6
103107-47-7 103107-48-8 103107-49-9 103107-50-2
103107-51-3 103107-52-4 103107-53-5 103107-54-6
103107-55-7 103107-56-8 103107-57-9 103107-58-0
103107-59-1 103107-60-4 103107-61-5 103107-62-6
103107-63-7 103107-64-8 103107-65-9 103107-66-0
103107-67-1 103107-68-2 103107-69-3 103107-70-6
103107-71-7 103107-72-8 103107-73-9 103107-74-0
103107-75-1 103107-76-2 103107-77-3 103107-78-4
103107-79-5 103107-80-8 103107-81-9 103107-82-0
103107-83-1 103107-84-2 103107-85-3 103107-86-4
103107-87-5 103107-88-6 103255-42-1
(amino acid sequence of)

INDEX TERM: 9003-53-6
(beads, in tumor necrosis factor isolation and purifn.)

INDEX TERM: 107-21-1, biological studies 9003-53-6D, quaternary amino-substituted 9012-36-6D, quaternary ammonium group-substituted 9013-34-7 12627-13-3
(in tumor necrosis factor isolation and purifn.)

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L1          2639 SEA FILE=HCA (ALPHA(1A)INTERFERON)/IT
L2            29 SEA FILE=HCA HAUPTMANN RUDOLF/AU
L3             6 SEA FILE=HCA L1 AND L2
L10       131526 SEA FILE=HCA (ESCHERICHIA COLI OR E COLI)/IA,IT,ST
L21         4930 SEA FILE=HCA (ALPHA(1A)INTERFERON)/IA,IT,ST
L22         4930 SEA FILE=HCA (142192-09-4 OR 142192-09-4D OR 142192-09-4P
                 )/IA,IT,ST OR L21
L23          360 SEA FILE=HCA L22 AND L10
L24          354 SEA FILE=HCA L23 NOT L3
L26          496 SEA FILE=HCA (PHOA OR ALKALINE(2A)PHOSPHATASE(2A)PROMOTER
                 #)/IA,IT,ST
L27            1 SEA FILE=HCA L24 AND L26
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L27 ANSWER 1 OF 1 HCA COPYRIGHT 1995 ACS
ACCESSION NUMBER: 103:17753 HCA
TITLE: Secretion of human **interferon-alpha**. induced by using secretion vectors containing a promoter and signal sequence of alkaline phosphatase gene of **Escherichia coli**
AUTHOR(S): Miyake, Tetsuo; Oka, Takanori; Nishizawa, Tsutomu; Misoka, Fusakazu; Fuwa, Toru; Yoda, Koji; Yamasaki, Makari; Tamura, Gakuzo
CORPORATE SOURCE: Cent. Res. Lab., Wakunaga Pharm. Co., Ltd., Hiroshima, 729-64, Japan
SOURCE: J. Biochem. (Tokyo) (1985), 97(5), 129-36
CODEN: JOBIAO; ISSN: 0021-924X
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 3-4 (Biochemical Genetics)
Section cross-reference(s): 13

ABSTRACT:
A new vector was constructed which contains the promoter and the signal sequence of the **E. coli phoA** gene, the structural gene for the periplasmic alk. phosphatase [9001-78-9]. One of the most useful characteristics of this vector is the unique HindIII restriction site located just at the end of the **phoA** signal sequence. This restriction site was generated by oligonucleotide-directed site-specific mutagenesis without changing the amino acid sequence of the signal peptide. Any kind of foreign structural gene can be easily inserted into the HindIII site by using synthetic oligonucleotides to construct a hybrid gene which has neither an extra

ordered 1cc 8/31

sequence nor a deletion between the **phoA** signal sequence and the foreign structural gene. Human **.alpha.-interferon** gene was inserted into this HindIII site. When this hybrid gene was expressed under the control of the **phoA** promoter region, a low but significant activity was recovered in the cold water wash of the cells after an osmotic shock procedure.

SUPPL. TERM: **interferon alpha** gene cloning
Escherichia; alk phosphatase interferon gene cloning vector; human interferon gene cloning Escherichia

INDEX TERM: **Escherichia coli**
(cloning in, of **.alpha.-interferon** gene of human)

INDEX TERM: Gene and Genetic element, animal
(for **.alpha.-interferon**, of human, cloning in **Escherichia coli** of)

INDEX TERM: Molecular cloning
(of **.alpha.-interferon** gene, of human, in **Escherichia coli**)

INDEX TERM: Gene and Genetic element, microbial
(promoter, for alk. phosphatase, of **Escherichia coli**, in human **.alpha.-interferon** gene expression)

INDEX TERM: Biological transport
(secretion, of **.alpha.-interferon**, of human, from **Escherichia coli**, alk. phosphatase signal sequence in)

INDEX TERM: Interferons
(.alpha.-, gene for, of human, cloning in **Escherichia coli** of)

INDEX TERM: Gene and Genetic element, microbial
(phaA, promoter of, of **Escherichia coli**, in human **.alpha.-interferon** gene expression)

INDEX TERM: 9001-78-9
(promoter and signal sequence for, of **Escherichia coli**, in human **.alpha.-interferon** gene expression)

```
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DISPLAY L# IS NOT VALID IN STNINDEX

COMMAND STACK INTERRUPTED.  ENTER "DISPLAY HISTORY"
TO SEE WHICH COMMANDS WERE EXECUTED.

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CLUSTER NAME      CLUSTER DEFINITION
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.BIO              MEDLINE HCA EMBASE BIOSIS WPIDS IFIPAT BIOTECHDS
                  DISSABS CONFSCI LIFESCI SCISEARCH JAPIO
                  JICST-EPLUS


L28               QUE  (142192-09-4 OR ALPHA(1A) INTERFERON)
L29               QUE  L28 AND (ESCHERICHIA COLI OR E COLI)
L30               QUE  (HEAT(2A) STABLE(2A) TOXIN# OR STII OR ST11 OR STABL
                  E(2A) ENTEROTOXIN#)
L31               QUE  L29 AND L30
L32               QUE  (PHOA OR ALKALINE(2A) PHOSPHATASE(2A) PROMOTER) AND
                  L29
L33               QUE  L31 OR L32


F1            2   MEDLINE
F2            2   EMBASE
F3            2   BIOTECHDS
F4            1   BIOSIS
F5            1   WPIDS
F6            1   LIFESCI
F7            1   SCISEARCH


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=> d que l43
L28               QUE  (142192-09-4 OR ALPHA(1A) INTERFERON)
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L29             QUE  L28 AND (ESCHERICHIA COLI OR E COLI)
L30             QUE  (HEAT(2A) STABLE(2A) TOXIN# OR STII OR ST11 OR STABL
                E(2A) ENTEROTOXIN#)
L31             QUE  L29 AND L30
L32             QUE  (PHOA OR ALKALINE(2A) PHOSPHATASE(2A) PROMOTER) AND
                L29
L33             QUE  L31 OR L32
L34           2 SEA FILE=MEDLINE L31 OR L32
L35           2 SEA FILE=EMBASE L31 OR L32
L36           2 SEA FILE=BIOTECHDS L31 OR L32
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L38           1 SEA FILE=WPIDS L31 OR L32
L39           1 SEA FILE=LIFESCI L31 OR L32
L40           1 SEA FILE=SCISEARCH L31 OR L32
L41          10 SEA L33
L42           3 DUP REM L41 (7 DUPLICATES REMOVED)
L43           3 SOR L42 PY
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=> d bib ab 1-

L43 ANSWER 1 OF 3 BIOTECHDS COPYRIGHT 1995 DERWENT INFORMATION LTD
AN 95-01432 BIOTECHDS
TI **Interferon-alpha** production in **Escherichia coli** with periplasmic secretion; protein secretion and purification; DNA sequence and protein sequence
AU Hauptmann R; Falkner E; Bodo G; Voss T; Maurer-Fogy I
PA Boehr.Ingelheim
PI EP-626448 30 Nov 1994
AI 94EP-0107804 19 May 1994
PRAI 93DE-4329756 3 Sep 1993; 93DE-431745P 26 May 1993
DT Patent
LA German
OS WPI: 95-000932 [01]
AB Production of **interferon-alpha** (I) in **Escherichia coli** involves growing cells that contain a vector in which the signal peptide (A) of the gene for **E. coli** thermostable enterotoxin-II (**STII**) is coupled to a sequence (B) encoding human mature (I). The following are also claimed: purification of (I) by adsorption chromatography on silica gel, hydrophobic interaction chromatography, cation-exchange chromatography and anion-exchange chromatography; and vectors for expressing (I) where (A) is linked to (B). Attachment of (A) to (B) ensures a stable expression system that ensures correctly folded protein secretion into the periplasmic space. Preferably, the vector includes a promoter from the **E. coli** alkaline phosphatase gene and a ribosome binding site from the **STII** gene. (B) preferably encodes **interferon-alpha**-2c of specified protein sequence. The 879 bp DNA sequence encoding this peptide preceded by the **STII** signal peptide is specified. When the (A)-(B) construct is used under the control of the **alkaline phosphatase promoter**, expression can be controlled by altering the phosphate level in the culture medium. (28pp)

L43 ANSWER 2 OF 3 MEDLINE
AN 85289134 MEDLINE
TI Secretion of human **interferon-alpha** induced by using secretion vectors containing a promoter and signal sequence of alkaline phosphatase gene of **Escherichia coli**.
AU Miyake T; Oka T; Nishizawa T; Misoka F; Fuwa T; Yoda K; Yamasaki M; Tamura G
SO J Biochem (Tokyo), (1985 May) 97 (5) 1429-36.
Journal code: HIF. ISSN: 0021-924X.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 8512
AB We constructed a new vector containing the promoter and the signal sequence of **E. coli phoA** gene, the structural gene for the periplasmic alkaline phosphatase. One of the most useful characteristics of this vector is the unique HindIII

restriction site located just at the end of the **phoA** signal sequence. This restriction site was generated by oligonucleotide-directed site-specific mutagenesis without changing the amino acid sequence of the signal peptide. Any kind of foreign structural gene can be easily inserted into the HindIII site by using synthetic oligonucleotides to construct a hybrid gene which has neither an extra sequence nor a deletion between the **phoA** signal sequence and the foreign structural gene. Human **alpha-interferon** gene was inserted into this HindIII site. When this hybrid gene was expressed under the control of the **phoA** promoter region, a low but significant activity was recovered in the cold water wash of the cells after an osmotic shock procedure.

L43 ANSWER 3 OF 3 MEDLINE
AN 94190282 MEDLINE
TI Periplasmic expression of human **interferon-alpha** 2c in **Escherichia coli** results in a correctly folded molecule.
AU Voss T; Falkner E; Ahorn H; Krystek E; Maurer-Fogy I; Bodo G; Hauptmann R
CS Ernst-Boehringer Institut fur Arzneimittelforschung, Bender & Co., Vienna, Austria.
SO Biochem J, (1994 Mar 15) 298 Pt 3 719-25.
Journal code: 9YO. ISSN: 0264-6021.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 9406
AB Human **interferon-alpha** 2c (IFN-alpha 2c) was produced in **Escherichia coli** under the control of the **alkaline phosphatase promoter** using a periplasmic expression system. Compared with other leader sequences, the heat-**stable enterotoxin** II leader of **E. coli** (**STII**) resulted in the highest rate of correct processing as judged by Western-blot analysis. The fermentation was designed as a batch-fed process in order to obtain a high yield of biomass. The processing rate of IFN-alpha 2c could be increased from 25% to more than 50% by shifting the fermentation pH from 7.0 to 6.7. IFN-alpha 2c extracted from the periplasm was purified by a new four-step chromatographic procedure. Whereas cytoplasmically produced IFN-alpha 2c does not have its full native structure, IFN-alpha 2c extracted from the periplasm was found to be correctly folded, as shown by c.d. spectroscopy. Peptide-map analysis in combination with m.s. revealed the correct formation of disulphide bridges. N-terminal sequence analysis showed complete removal of the leader sequence, creating the authentic N-terminus starting with cysteine.

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=> file hom;d his
FILE 'HOME' ENTERED AT 15:18:38 ON 30 AUG 95


     (FILE 'HOME' ENTERED AT 14:40:23 ON 30 AUG 95)
                SET PAGELENGTH SCROLL

     FILE 'REGISTRY' ENTERED AT 14:41:00 ON 30 AUG 95
                E INTERFEREON ALPHA/CN
                E INTERFERON ALPHA/CN
                E ALPHA INTERFERON/CN

     FILE 'HCA' ENTERED AT 14:41:58 ON 30 AUG 95
L1          2639 S (ALPHA(1A)INTERFERON)/IT
                 E HAUPTMANN RUDOLF/AU
L2            29 S HAUPTMANN RUDOLF/AU
L3             6 S L1 AND L2
L4         29763 S INTERFERON#/IA,IT,ST

     FILE 'HOME' ENTERED AT 14:46:41 ON 30 AUG 95

     FILE 'HCA' ENTERED AT 14:49:01 ON 30 AUG 95
L5         33396 S PLASMID AND EPISOME/IT
L6         61528 S L5 OR (PLASMID# OR EPISOME#)/IA,IT,ST
L7           984 S L4 AND L6
L8             3 S L7 AND (142192-09-4 OR 142192-09-4D OR 142192-09-4P)
L9             2 S L8 NOT L3

     FILE 'HCA' ENTERED AT 14:51:45 ON 30 AUG 95
L10       131526 S (ESCHERICHIA COLI OR E COLI)/IA,IT,ST
L11         1366 S L4 AND L10
L12        53776 S (TOXIN#)/IA,IT,ST
L13           87 S L11 AND L12
L14       524215 S (HEAT(2A)STABLE(2A)TOXIN# OR ST## OR STABLE(2A)ENTEROTO
L15            7 S L13 AND L14
L16            6 S L15 NOT L3
L17          884 S (HEAT(2A)STABLE(2A)TOXIN# OR STII OR ST11 OR STABLE(2A)
L18            3 S L13 AND L17
L19            2 S L18 NOT L3
L20            2 SORT L19 PY

     FILE 'HCA' ENTERED AT 14:58:20 ON 30 AUG 95
L21         4930 S (ALPHA(1A)INTERFERON)/IA,IT,ST
L22         4930 S (142192-09-4 OR 142192-09-4D OR 142192-09-4P)/IA,IT,ST
L23          360 S L22 AND L10
L24          354 S L23 NOT L3
L25            0 S L24 AND L17
L26          496 S (PHOA OR ALKALINE(2A)PHOSPHATASE(2A)PROMOTER#)/IA,IT,ST
L27            1 S L24 AND L26

     FILE 'HCA' ENTERED AT 15:03:54 ON 30 AUG 95

     INDEX 'MEDLINE, HCA, EMBASE, BIOSIS, WPIDS, IFIPAT, BIOTECHDS,
     DISSABS, CONFSCI, LIFESCI, SCISEARCH, JAPIO, JICST-EPLUS' ENTERED
     AT 15:05:00 ON 30 AUG 95
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     INDEX 'MEDLINE, EMBASE, BIOSIS, WPIDS, IFIPAT, BIOTECHDS, DISSABS,
     CONFSCI, LIFESCI, SCISEARCH, JAPIO, JICST-EPLUS' ENTERED AT
     15:05:06 ON 30 AUG 95
                SEA (ALPHA(1A)INTERFERON)
               ---------
            8199   FILE MEDLINE
                SEA (142192-09-4 OR ALPHA(1A)INTERFERON)
               ---------
            8199   FILE MEDLINE
           12810   FILE EMBASE
           11773   FILE BIOSIS
             320   FILE WPIDS
             143   FILE IFIPAT
             702   FILE BIOTECHDS
             131   FILE DISSABS
             429   FILE CONFSCI
            3011   FILE LIFESCI
            7671   FILE SCISEARCH
              59   FILE JAPIO
            2304   FILE JICST-EPLUS
L28             QUE (142192-09-4 OR ALPHA(1A) INTERFERON)
               ---------
                SEA L28 AND (ESCHERICHIA COLI OR E COLI)
               ---------
             182   FILE MEDLINE
             183   FILE EMBASE
             239   FILE BIOSIS
              36   FILE WPIDS
              13   FILE IFIPAT
             284   FILE BIOTECHDS
               3   FILE DISSABS
               5   FILE CONFSCI
              95   FILE LIFESCI
             105   FILE SCISEARCH
               3   FILE JAPIO
              12   FILE JICST-EPLUS
L29             QUE L28 AND (ESCHERICHIA COLI OR E COLI)
               ---------
                SEA (HEAT(2A)STABLE(2A)TOXIN# OR STII OR ST11 OR STABLE(2
               ---------
            1046   FILE MEDLINE
             829   FILE EMBASE
            1240   FILE BIOSIS
              33   FILE WPIDS
              15   FILE IFIPAT
              71   FILE BIOTECHDS
              48   FILE DISSABS
              49   FILE CONFSCI
             507   FILE LIFESCI
             757   FILE SCISEARCH
              49   FILE JAPIO
              57   FILE JICST-EPLUS
L30             QUE (HEAT(2A) STABLE(2A) TOXIN# OR STII OR ST11 OR STABLE
               ---------
                SEA L29 AND L30
               ---------
```

```
                1   FILE MEDLINE
                1   FILE EMBASE
                1   FILE BIOSIS
                1   FILE WPIDS
                1   FILE BIOTECHDS
                1   FILE SCISEARCH
L31              QUE L29 AND L30
                ---------
                 SEA (PHOA OR ALKALINE(2A)PHOSPHATASE(2A)PROMOTER) AND L29
                ---------
                2   FILE MEDLINE
                2   FILE EMBASE
                1   FILE BIOSIS
                1   FILE WPIDS
                2   FILE BIOTECHDS
                1   FILE LIFESCI
                1   FILE SCISEARCH
L32              QUE (PHOA OR ALKALINE(2A) PHOSPHATASE(2A) PROMOTER) AND L
                ---------
                 SEA L31 OR L32
                ---------
                2   FILE MEDLINE
                2   FILE EMBASE
                1   FILE BIOSIS
                1   FILE WPIDS
                2   FILE BIOTECHDS
                1   FILE LIFESCI
                1   FILE SCISEARCH
L33              QUE L31 OR L32
                ---------

     FILE 'MEDLINE, EMBASE, BIOTECHDS, BIOSIS, WPIDS, LIFESCI,
     SCISEARCH' ENTERED AT 15:15:03 ON 30 AUG 95
     FILE 'MEDLINE'
L34              2 S L33
     FILE 'EMBASE'
L35              2 S L33
     FILE 'BIOTECHDS'
L36              2 S L33
     FILE 'BIOSIS'
L37              1 S L33
     FILE 'WPIDS'
L38              1 S L33
     FILE 'LIFESCI'
L39              1 S L33
     FILE 'SCISEARCH'
L40              1 S L33
     TOTAL FOR ALL FILES
L41             10 S L33
L42              3 DUP REM L41 (7 DUPLICATES REMOVED)
L43              3 SORT L42 PY

     FILE 'HOME' ENTERED AT 15:18:38 ON 30 AUG 95
```